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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,615	01/03/2002	Stacie J. Casman	21402-233 (Cura533)	5238

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EXAMINER	
KEMMERER, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,615	CASMAN ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 0200*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

Applicant's election of Group II (claims 5-14) and Group Q (SEQ ID NOS: 33 and 34) in the "RESPONSE TO OCTOBER 17, 2003 RESTRICTION REQUIREMENT" received 10 December 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Application, Amendments, And/Or Claims

The preliminary amendments received 29 January 2003 and 10 December 2003 have been entered in full. Claims 1-4 and 15-52 are canceled. Claims 5-14 are under examination.

Specification

The disclosure is objected to because of the following informalities: The specification attributes two distinct sequences to SEQ ID NO: 34. See p. 30, wherein SEQ ID NO: 34 is attributed to nucleic acid encoding GPCR4a, whereas at p. 98, SEQ ID NO: 34 is disclosed as being the amino acid sequence of GPCR16.

Appropriate correction is required.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 10, 11 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 5, it is not clear what is meant by "a mature form" of a particular polypeptide. Are there more than one possible mature form for each recited polypeptide? Neither the specification nor the art make this clear. Since the structures of the recited polypeptides cannot be envisioned, the metes and bounds of the claimed invention cannot be determined and the claim is indefinite. Amending the claim to recite "**the** mature form" would obviate this issue.

Also in claim 5, the following is unclear: "...comprising an **amino acid sequence** selected from the group consisting of: ...(e) a **nucleic acid fragment**... and (f) a **nucleic acid molecule**...". An amino acid sequence cannot also be a nucleic acid sequence.

Claim 10 recites hybridization under stringent conditions. Neither the specification nor the art provide an unambiguous definition for this term. The term is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 10 and 11 recite "or a complement of said nucleotide sequence". This is indefinite since it implies that there is more than one possible complementary sequence.

Are fragments of the full-length complement intended? Amending the claim to recite "or **the** complement" would obviate this issue.

Claim 14 is directed to a cell comprising a vector. It is unclear if an isolated host cell is intended or a transformed cell in the context of a multicellular organism is intended. Clarification is required. Amending the claim to recite "An **isolated** host cell" would render the claim clear.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-14 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to isolated nucleic acids encoding SEQ ID NO: 34 (GPCR16) or fragments or variants thereof, vectors comprising same, and host cells comprising same. The specification discloses that the polypeptide of SEQ ID NO: 34 has 56% homology to EBV-induced G protein coupled receptor 2. Based on this structural similarity, the specification asserts several utilities for the claimed invention. However, none of the utilities asserted by the specification meet the three-pronged test

of being credible, specific and substantial. Each asserted utility will be addressed in turn:

1) The claimed nucleic acids are useful in that they encode an EBV-induced GPCR2-like protein, which is expected to have biological activities similar to EBV-induced GPCR2. This asserted utility is credible and specific, but it is not substantial. The polypeptide encoded by the claimed nucleic acids has 56% homology to prior art polypeptide EBV-induced GPCR2. However, the art also recognizes that the GPCR family of polypeptides, while very similar structurally, are functionally diverse. For example, Ji et al. (1998, J. Biol. Chem. 273:17299-17302) disclose that all GPCRs have the general structure of an extracellular N-terminal segment, seven transmembrane spanning domains, three exoloops, three-four cytoloops and a C-terminal segment (p. 17299). Despite this, the GPCR members show diverse modes of ligand binding, signal generation, transmembrane signal transduction and signal transfer to various cytoplasmic signal molecules such as G proteins, Jak2 kinase, phospholipase Cγ and protein kinase C (p. 17302). Murdoch et al. (2000, Blood 95 :3032-3043) disclose that the GPCR subfamily of chemokine receptors have strong structural similarity, however, there is still great functional diversity even within this subfamily due to the receptors being expressed on different cell types and their binding distinct ligands(see Abstract).

In general, the art recognizes that function cannot be predicted based solely on structural similarities to sequences found in sequence databases (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997,

Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Neither the specification no the prior art disclose SEQ ID NO: 34's ligand or physiological significance. The prior art clearly indicates that significant further research would be required by the skilled artisan to identify such, and thus the asserted utility is not a "real world" use, and is not substantial.

2) The claimed nucleic acids or the encoded polypeptide can be used in the diagnosis, prognosis, or treatment of disease or tissue regeneration. This asserted utility is also credible, but not specific or substantial. Since a mutation in any gene can lead to disease, every gene is a potential target for diagnostics or drug development. Also, the asserted utility is not substantial, since neither the specification nor the prior art disclose a nexus between any specific disease state and a change in SEQ ID NO: 33 or 34 levels, form, or expression patterns. Significant further research would be required of the skilled artisan to determine such a nexus. Thus the asserted utility is not a real world use, and is not substantial. As evidence of this, please see Sades et al. (2001, AAPS PharmSci 3 (3): article 22) who state that therapeutic relevance of new and variants GPCR sequences remains unclear (p. 1).

3) The claimed nucleic acids or the encoded polypeptide can be used as cell or tissue specific markers, to screen for agonists/antagonists, in assays to detect the presence of SEQ ID NO: 34, chromosome mapping, SNP determination, biological weapon development and generation of transgenic animals. These asserted utilities are credible, but not specific or substantial. Such can be done with any nucleic acid or its

encoded polypeptide, and thus the asserted utilities are not specific to the claimed invention. Also, since the relevance of SEQ ID NO: 34 is not known, the relevance of agonists, antagonists, transgenic animals, chromosome mapping probes, and SNPs are also not known and would have to be determined empirically. The requirement for such additional research indicates that the asserted utilities are not substantial.

For all of these reasons, the disclosure fails to meet the requirements of 35 U.S.C. § 101 and the claims are rejected.

Claims 5-14 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Furthermore, the claims recite nucleic acids encoding fragments and variants of SEQ ID NO: 34. Such variants are also not enabled by the specification. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions

may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for an undefined activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and

function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claims 5-14 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to isolated nucleic acids encoding SEQ ID NO: 34 or fragments or variants thereof, vectors comprising same, and host cells comprising same.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity, hybridization, or other variant language. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 34, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acids encoding polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 34, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is

reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER